

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: M.L. Bayne et al.

Serial No.: To be assigned Case No. 18199CB

Filed: Submitted on even date herewith

For: DNA MOLECULES ENCODING VASCULAR  
ENDOTHELIAL CELL GROWTH FACTOR II  
SUBUNITS (As Amended Herein)

1646

Examiner:  
L. Spector

Assistant Commissioner of Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT, 37 C.F.R. §1.111, 1.115**

Sir:

Preliminary to the examination of this Rule 53(b) continuation application, please calculate the filing fee due based on entry of new claims 22-37. Please enter the additional amendments and consider the following remarks. This application is co-pending to U.S. Application Serial No. 09/326,879, filed June 7, 1999. A Notice of Appeal was filed in the '879 application on September 10, 2001. A Petition to Extend Time under 37 C.F.R. §1.136(a) for three (3) months is entered on an even date herewith to continue pendency of the '879 application up to and including Monday, February 11, 2002. Applicants intend to cease further prosecution of the '879 case in favor of this above-identified continuation application.

EXPRESS MAIL CERTIFICATE  
DATE OF DEPOSIT February 8, 2002  
EXPRESS MAIL NO EL523 909946 US  
I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS  
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FOR PATENTS, WASHINGTON, D.C., 20231.  
MAILED BY Christa Cuffe  
DATE 2-8-02

**IN THE SPECIFICATION:**

At page 1, line 2, please delete the title "VASCULAR ENDOTHELIAL CELL GROWTH FACTOR II" and insert a new title --DNA MOLECULES ENCODING VASCULAR ENDOTHELIAL CELL GROWTH FACTOR II SUBUNITS--.

At page 1, line 5, delete the continuing data and add the following continuing data:

-- This application is a continuation application of application no. 09/326,879, filed June 7, 1999, which is a divisional of application no. 09/038,199, filed March 10, 1998, issued as U.S. Patent No. 6,180,107, which is a divisional of application no. 08/299,185, filed August 31, 1994, issued as U.S. Patent No. 5,726,152, which is a continuation-in-part of application no. 08/000,834, filed January 5, 1993, abandoned, which is a continuation of application no. 07/586,638, filed September 21, 1990, abandoned. --.

At page 2, line 22, following "Figure 5", please insert --and Figures 5A through 5C--.

At page 2, line 26, following "Figure 6", please insert --and Figures 6A through 6B--.

At page 2, line 32 following "Figure 7", please insert --and Figure 7A--.

At page 10, line 22, please delete "Figure 4" and insert --Figures 4 through 4M--.

At page 11, line 5, please delete "Figure 4" and insert --Figures 4 through 4M--.

At page 11, line 11, please delete "Fig. 4 and Fig. 5" and insert --Figures 4 through 4M and Figures 5 through 5C--.

At page 11, line 27, please delete "Figure 4" and insert --Figures 4 through 4M--.

At page 11, line 33, please delete "Fig. 5 and Fig. 6" and insert --Figures 5 through 5C and Figures 6 through 6B--.

At page 12, line 5, please delete "Figs. 4 and 5" and insert --Figures 4 through 4M and Figures 5 through 5C--.

At page 13, line 3, please delete "Fig. 6 and Fig. 7" and insert --Figures 6 through 6B and Figures 7 through 7A--.

At page 23, line 15, please delete "Figs. 5 and 6" and insert -- --Figures 5 through 5C and Figures 6 through 6B--.

At page 23, line 16, please delete "Fig. 5" and insert --Figures 5 through 5C--.

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At page 23, line 17, please delete "Fig. 6" and insert --Figures 6 through 6B--.

At page 29, line 13, please delete "Fig. 5" and insert --Figures 5 through 5C--.

At page 37, line 25 please delete "Figures 6 and 7" and insert --Figures 6 through 6B and Figures 7 through 7A--.

At page 39, line 31, please delete "Fig. 6 and Fig. 7" and insert --Figures 6 through 6B and Figures 7 through 7A--.

At page 39, line 33, please delete "Fig. 7" and insert --Figures 7 through 7A--.

At page 40, line 1, please delete "Fig. 7" and insert --Figures 7 through 7A--.

At page 42, line 20, please delete "Fig. 6" and insert --Figures 6 through 6B--.

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**IN THE CLAIMS:**

Please cancel claims 1-21, without prejudice.

Please enter new claims 22-37, as follows:

22(New). A purified DNA molecule encoding a B subunit of vascular endothelial growth factor II wherein said B subunit comprises the 158 amino acid precursor protein as shown in Figure 6.

23(New). An expression vector for expressing a B subunit of vascular endothelial growth factor II in a recombinant host cell wherein said expression vector comprises a DNA molecule of claim 22.

24(New). A host cell which expresses a recombinant a B subunit of vascular endothelial growth factor II wherein said host cell contains the expression vector of claim 23.

25(New). A process for expressing a B subunit of vascular endothelial growth factor protein in a recombinant host cell, comprising:

(a) transfecting the expression vector of claim 23 into a suitable host cell;  
and,

(b) culturing the host cells of step (a) under conditions which allow expression of said B subunit of vascular endothelial growth factor protein from said expression vector.

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26(New). A purified DNA molecule encoding a B subunit of vascular endothelial growth factor II wherein said B subunit comprises the 135 amino acid mature protein as shown in Figure 6.

27(New). An expression vector for expressing a B subunit of vascular endothelial growth factor II in a recombinant host cell wherein said expression vector comprises a DNA molecule of claim 26.

28(New). A host cell which expresses a recombinant a B subunit of vascular endothelial growth factor II wherein said host cell contains the expression vector of claim 27.

29(New). A process for expressing a B subunit of vascular endothelial growth factor protein in a recombinant host cell, comprising:

(a) transfecting the expression vector of claim 27 into a suitable host cell;  
and,

(b) culturing the host cells of step (a) under conditions which allow expression of said B subunit of vascular endothelial growth factor protein from said expression vector.

30(New). A purified DNA molecule encoding a B subunit of vascular endothelial growth factor II wherein said B subunit comprises the 138 amino acid precursor protein as shown in Figure 7.

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31(New). An expression vector for expressing a B subunit of vascular endothelial growth factor II in a recombinant host cell wherein said expression vector comprises a DNA molecule of claim 30.

32(New). A host cell which expresses a recombinant a B subunit of vascular endothelial growth factor II wherein said host cell contains the expression vector of claim 31.

33(New). A process for expressing a B subunit of vascular endothelial growth factor protein in a recombinant host cell, comprising:

(a) transfecting the expression vector of claim 31 into a suitable host cell;  
and,

(b) culturing the host cells of step (a) under conditions which allow expression of said B subunit of vascular endothelial growth factor protein from said expression vector.

34(New). A purified DNA molecule encoding a B subunit of vascular endothelial growth factor II wherein said B subunit comprises the 115 amino acid mature protein as shown in Figure 7.

35(New). An expression vector for expressing a B subunit of vascular endothelial growth factor II in a recombinant host cell wherein said expression vector comprises a DNA molecule of claim 34.

36(New). A host cell which expresses a recombinant a B subunit of vascular endothelial growth factor II wherein said host cell contains the expression vector of claim 35.

37(New). A process for expressing a B subunit of vascular endothelial growth factor protein in a recombinant host cell, comprising:

(a) transfecting the expression vector of claim 35 into a suitable host cell;  
and,

(b) culturing the host cells of step (a) under conditions which allow expression of said B subunit of vascular endothelial growth factor protein from said expression vector.

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**REMARKS**

Original claims 1-21 are cancelled , without prejudice.

New claims 22-37 are respectfully entered. New claims 22-37 correspond to allowed subject matter from U.S. Application Serial No. 09/326,879, as follows:

	<u>'879 Application</u>	<u>New Claims</u>
Claim #	26	22
	27	23
	28	24
	29	25
	30	26
	31	27
	32	28
	33	29
	34	30
	35	31
	36	32
	37	33
	38	34
	39	35
	40	36
	41	37

The specification was amended in anticipation of utilizing the same formal drawings as used in U.S. Patent No. 5,726,152, as well as updating the continuing data. Applicants respectfully note that reference should be made to appl. no. 07/586,638, not 07/586,631.



New claims 22-37 mirror allowed claims from the '879 application as noted above. Applicants reserve the right to pursue non-elected and/or non-recited subject matter in a future continuing application. No new matter is added by entry of new claims 22-37. Applicants respectfully take the position that the pending claims remain allowable. If necessary, the Examiner is invited to contact the undersigned attorney by telephone if clarification is required on any aspect of this response.

Respectfully submitted,

By J. Mark Hand  
J. Mark Hand  
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Rahway, NJ 07065-0907  
(732) 594-3905

Date: FEBRUARY 8, 2002

2002 FEB 08 09:00

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	M. Bayne et al.	Art Unit:	1647
Serial No.:	09/326,879 – Case 18199CB	Examiner:	L. Spector
Filed:	Concurrently herewith (Express Mail EL523909946US)		
For:	VASCULAR ENDOTHELIAL CELL GROWTH FACTOR II		

Assistant Commissioner of Patents  
Washington, D.C. 20231

**ATTENTION: Official Draftsman**

TRANSMITTAL OF FORMAL DRAWINGS

Sir:

Submitted herewith are new drawings to correct the informalities in the originally submitted drawings. Enclosed please find thirty two (32) sheets of formal drawings (Figs 1-11).

Should communication with the undersigned representative facilitate the review and the acceptance of the enclosed drawings, the Official Draftsman is invited to telephone the representative at the number listed below.

Respectfully submitted,

By J. Mark Hand  
J. Mark Hand

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(732) 594-4720 - fax

EXPRESS MAIL CERTIFICATE

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FOR PATENTS, WASHINGTON, D.C., 20231.

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DATE 2-8-02

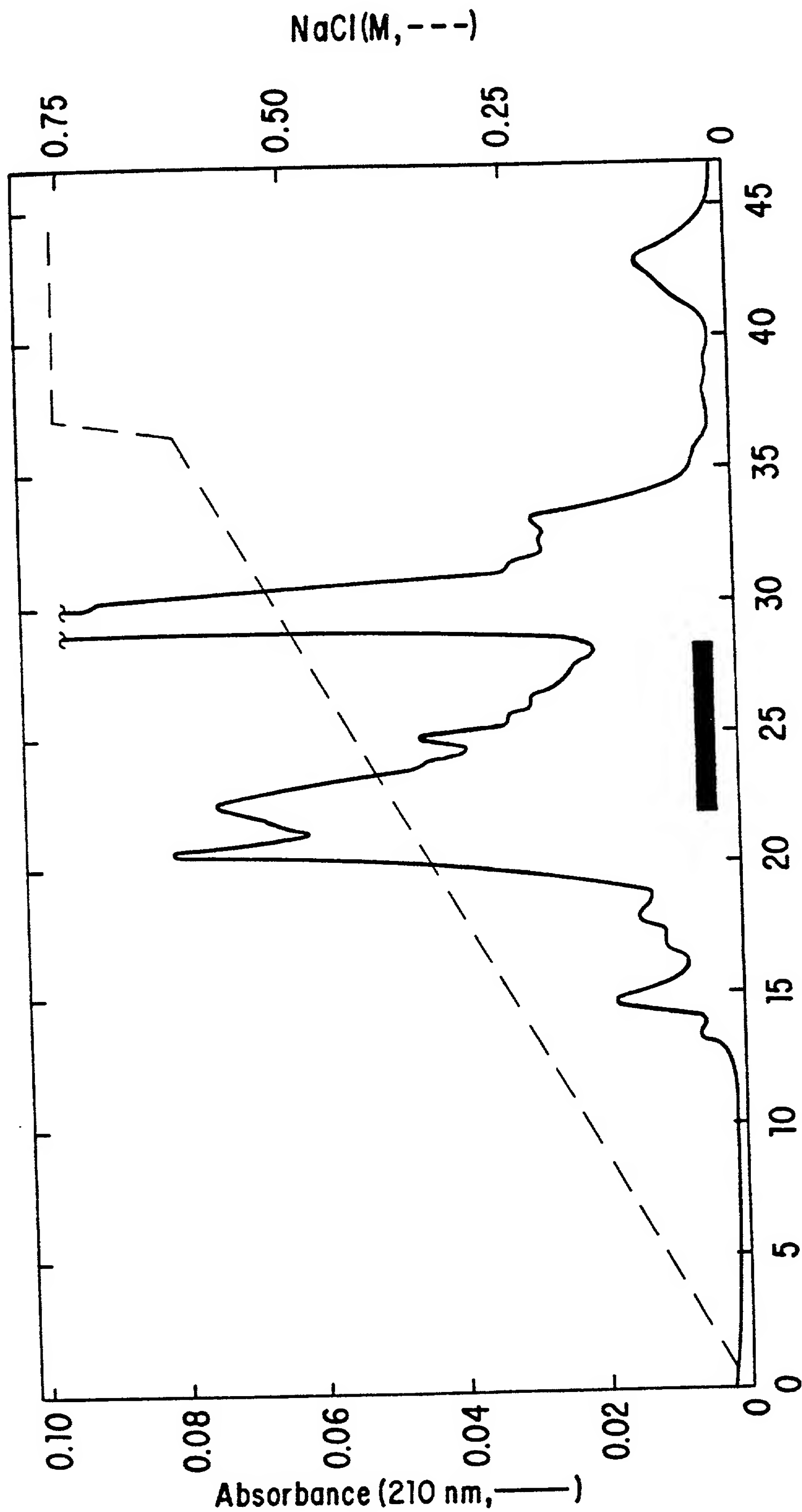


FIG. 1

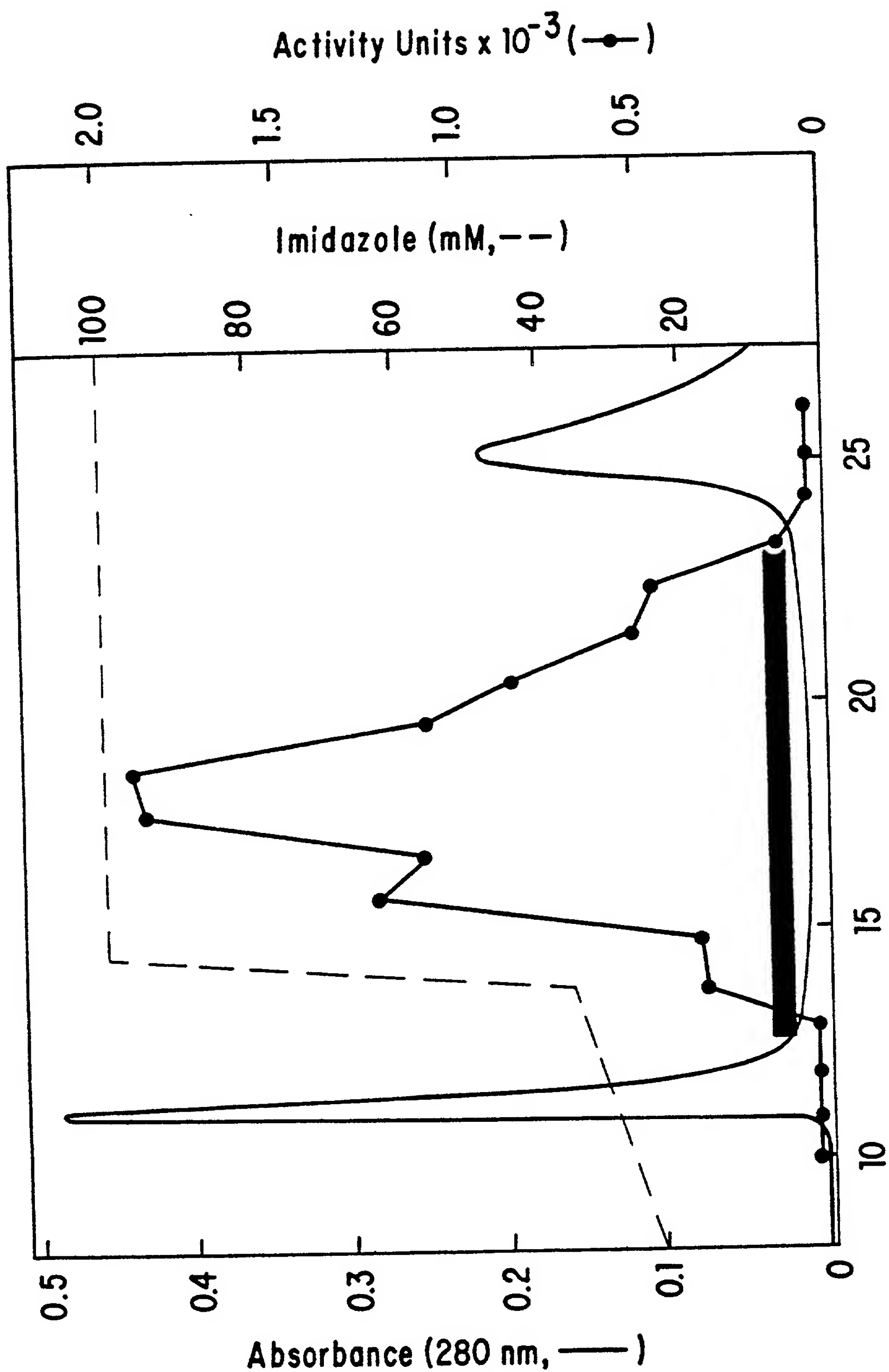


FIG. 2

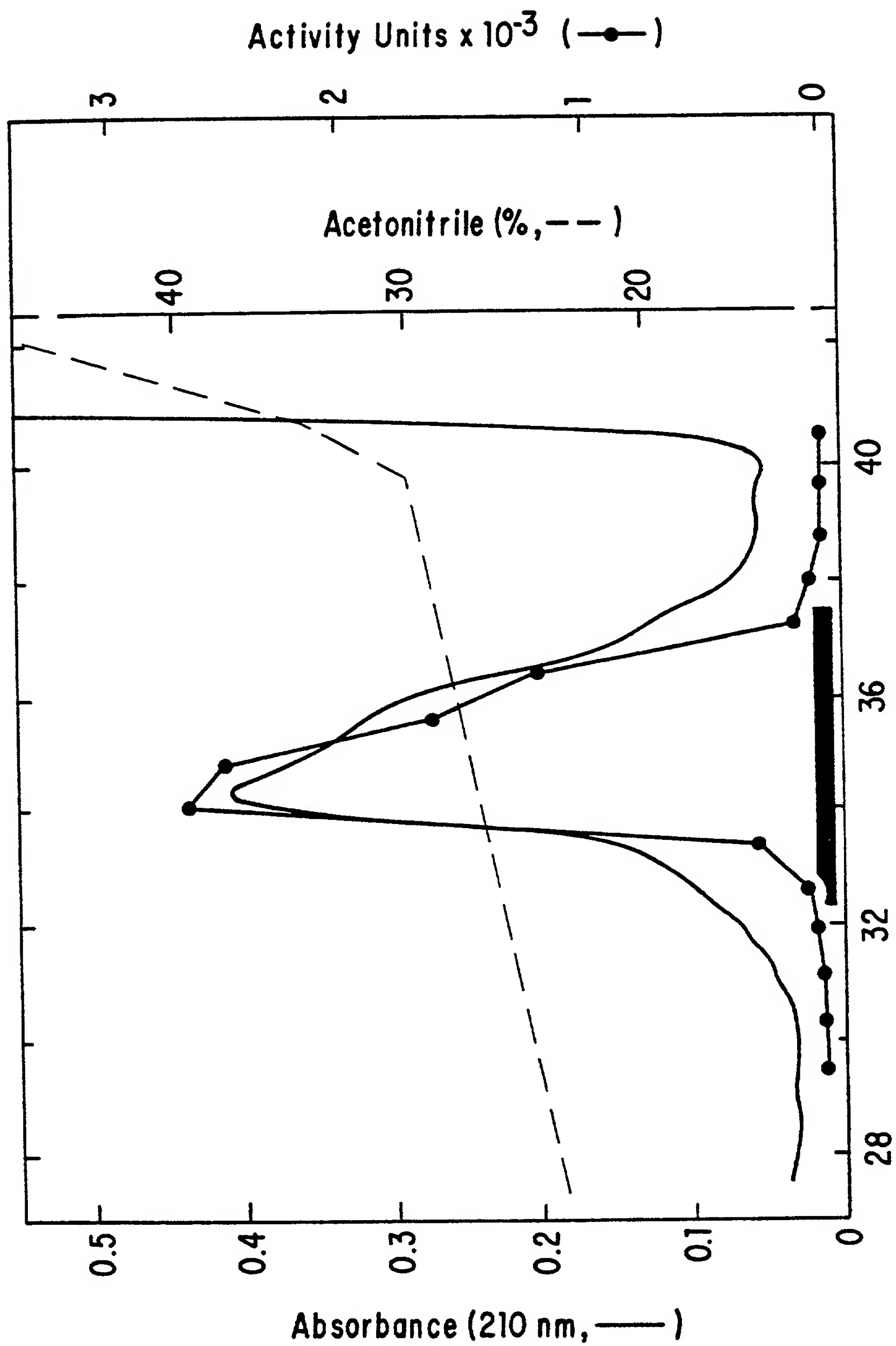
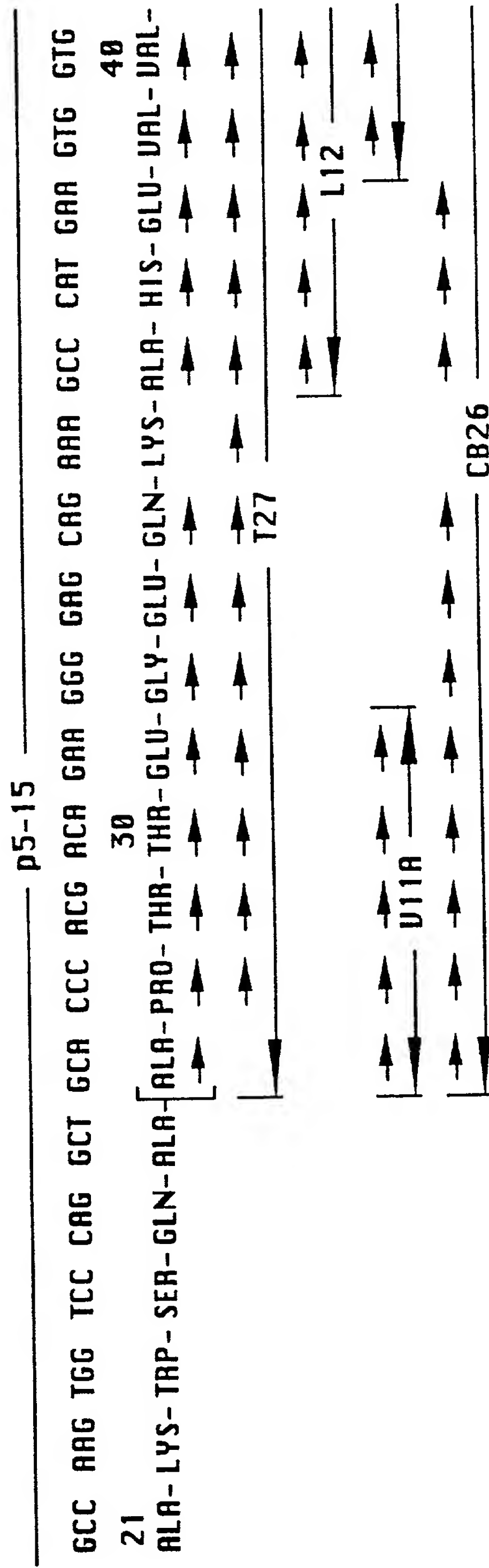


FIG. 3



81 7

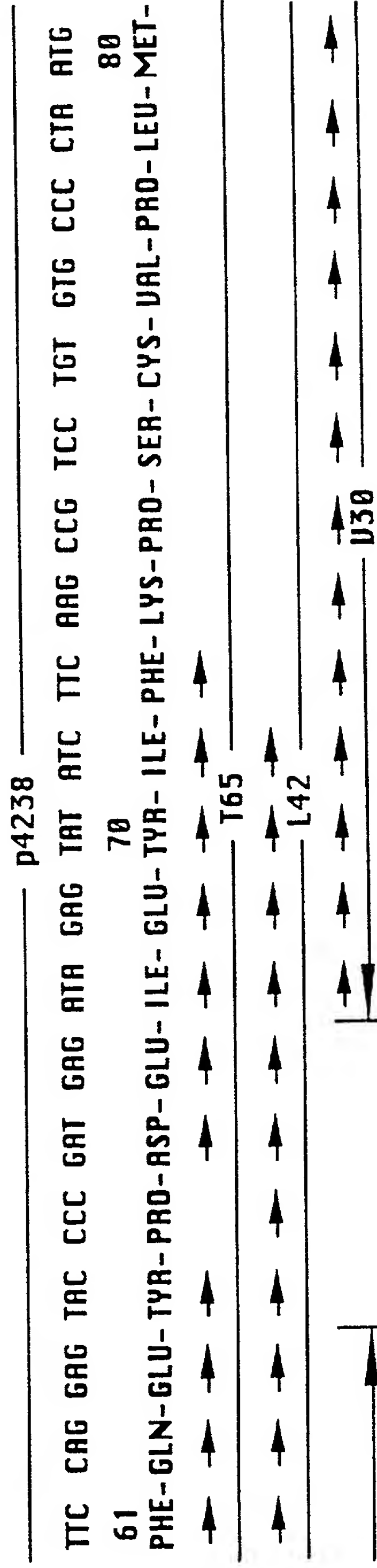
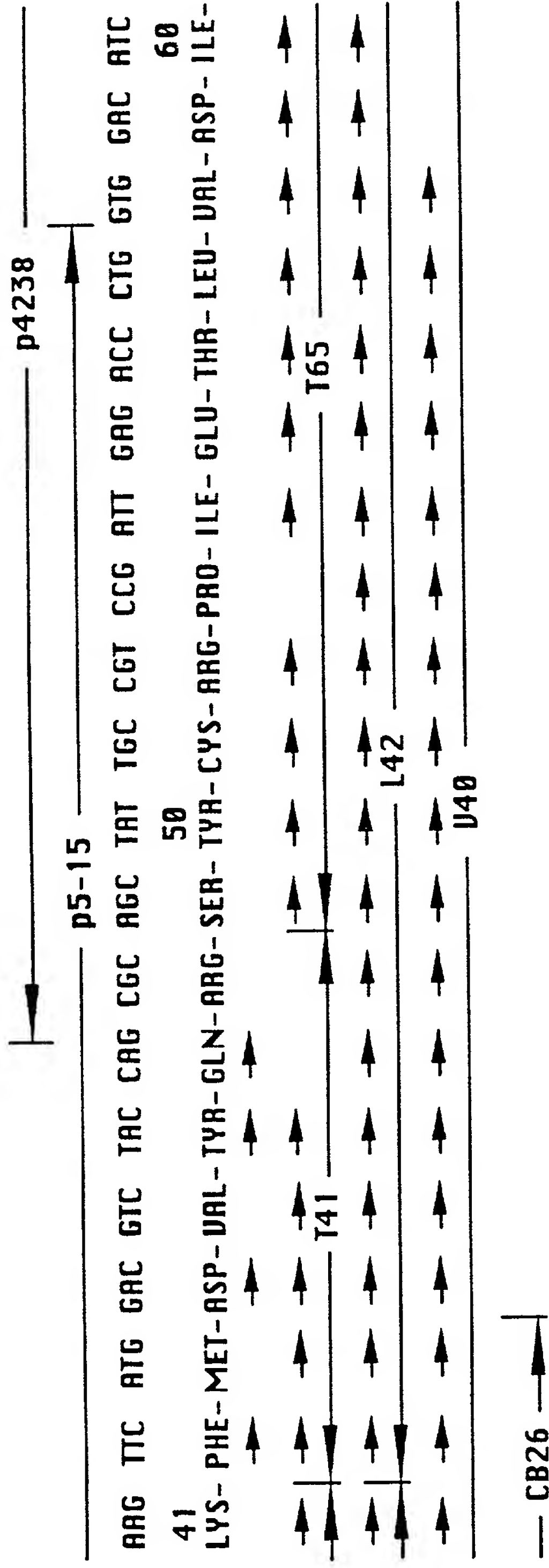


FIG. 4A

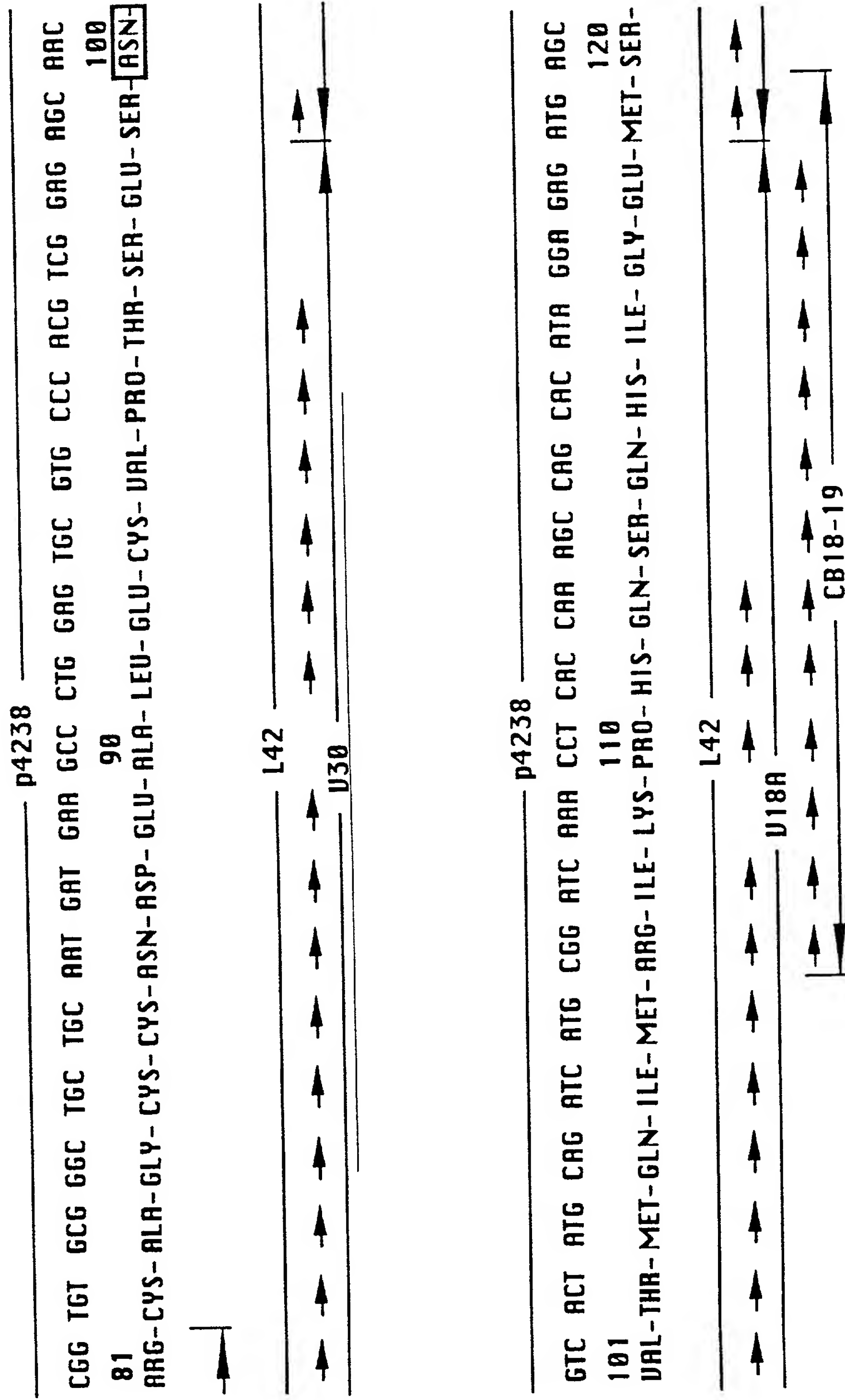
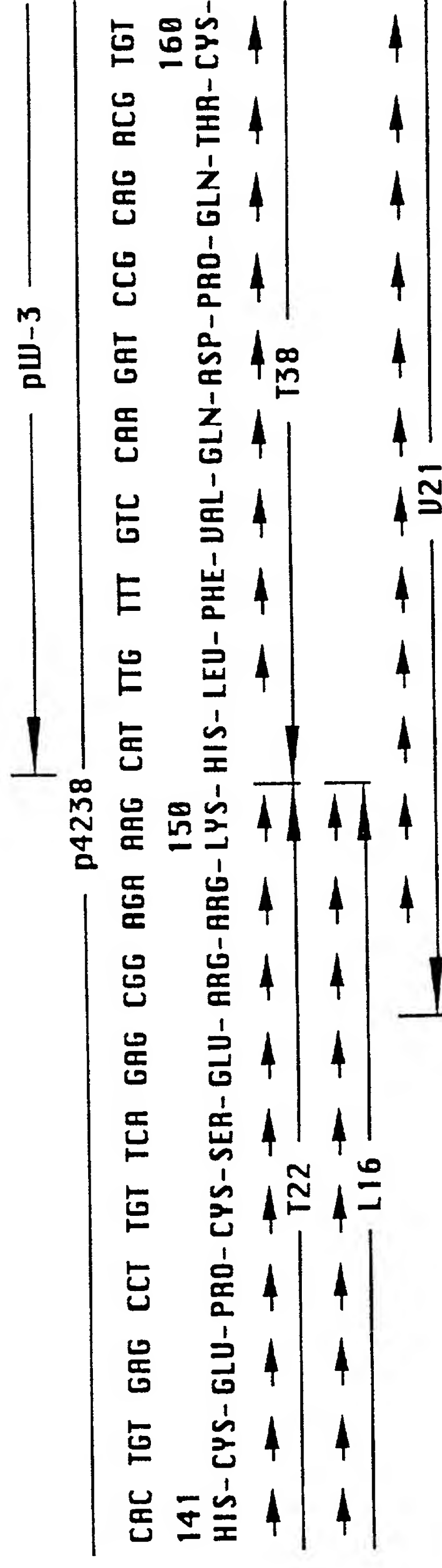
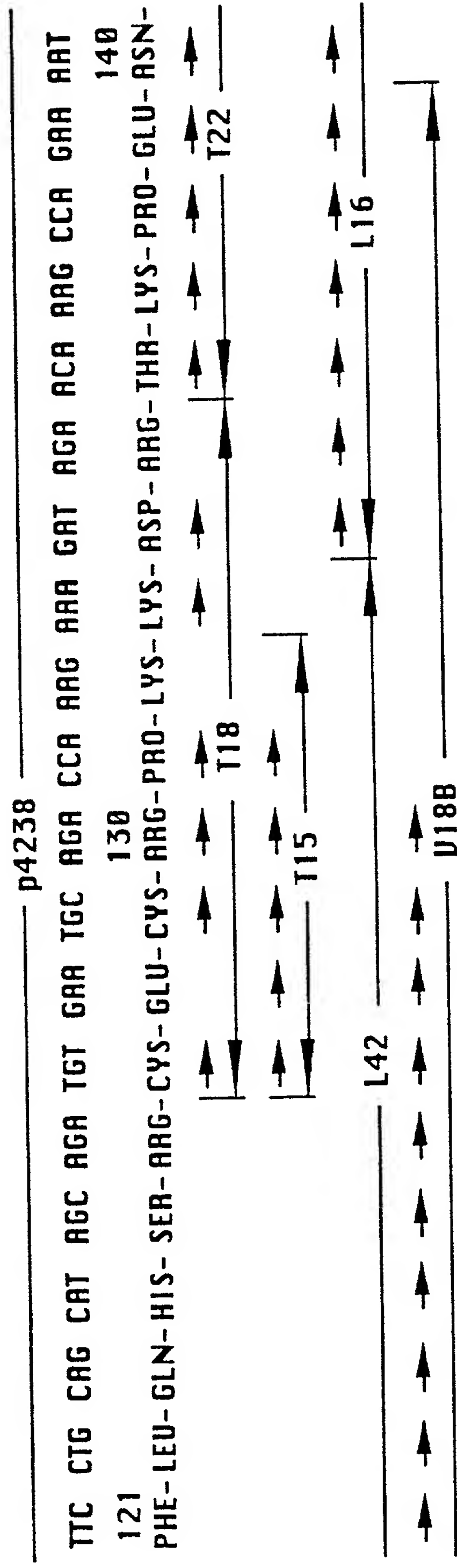


FIG. 4B





**FIG. 4C**

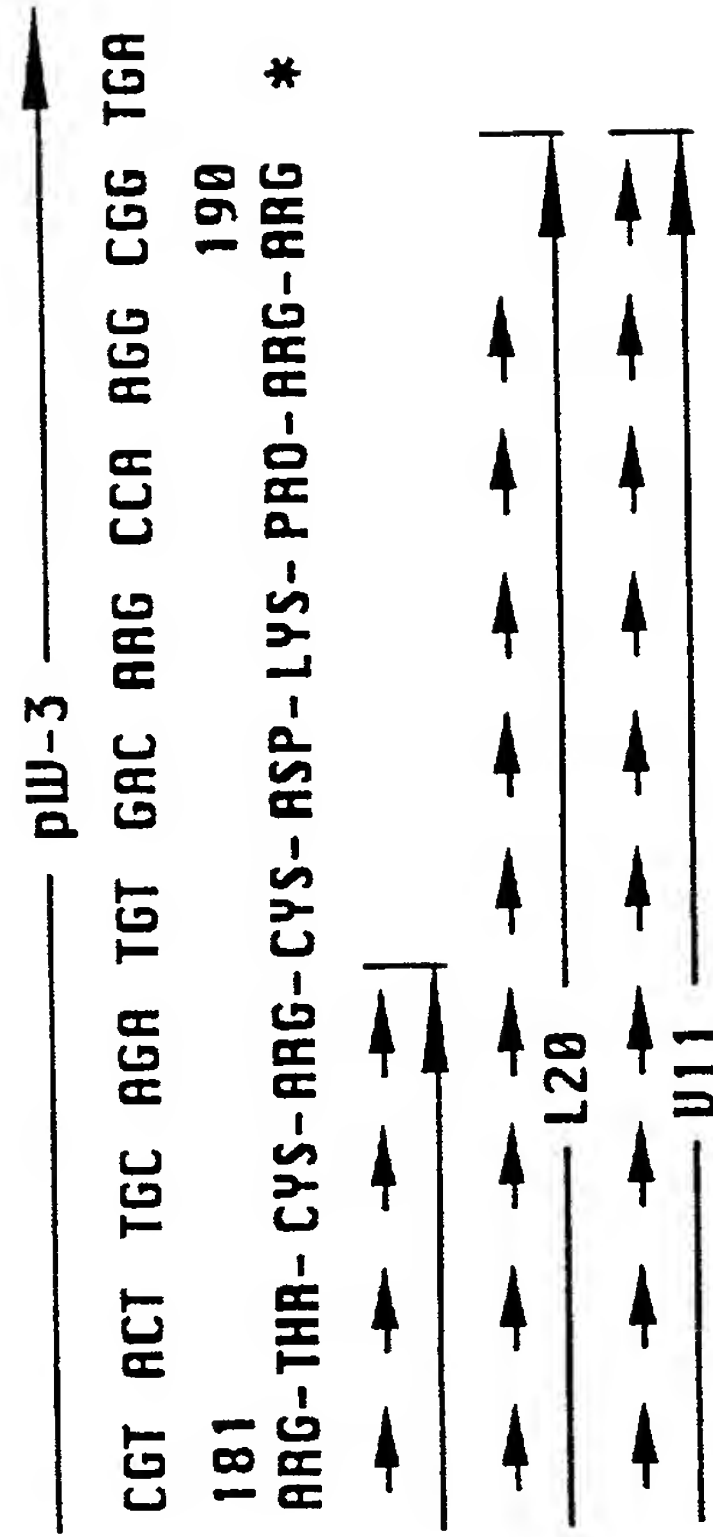
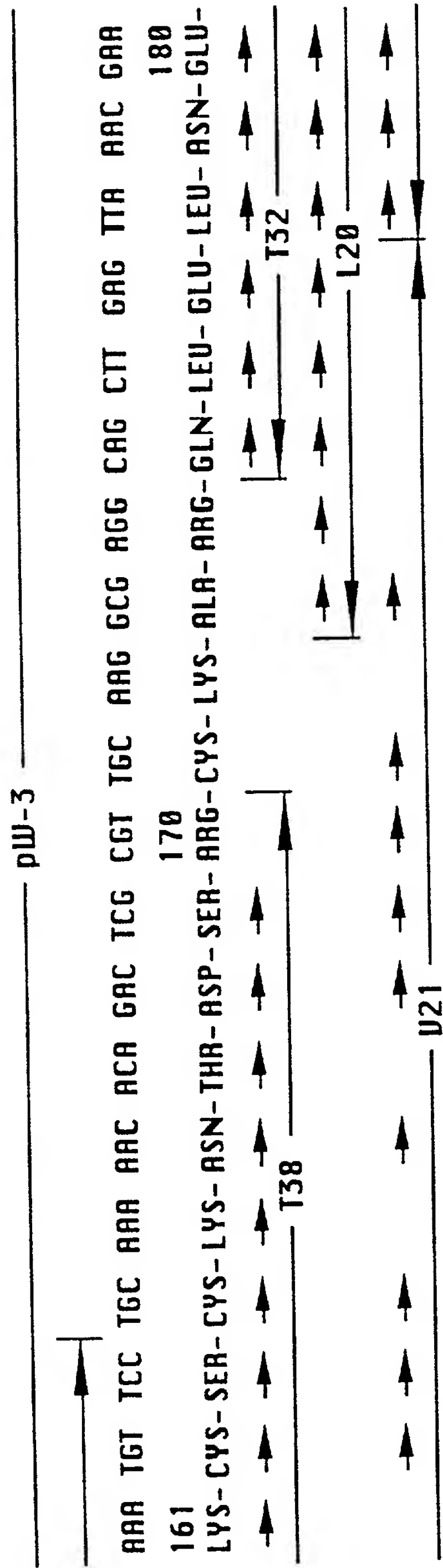


FIG. 4D

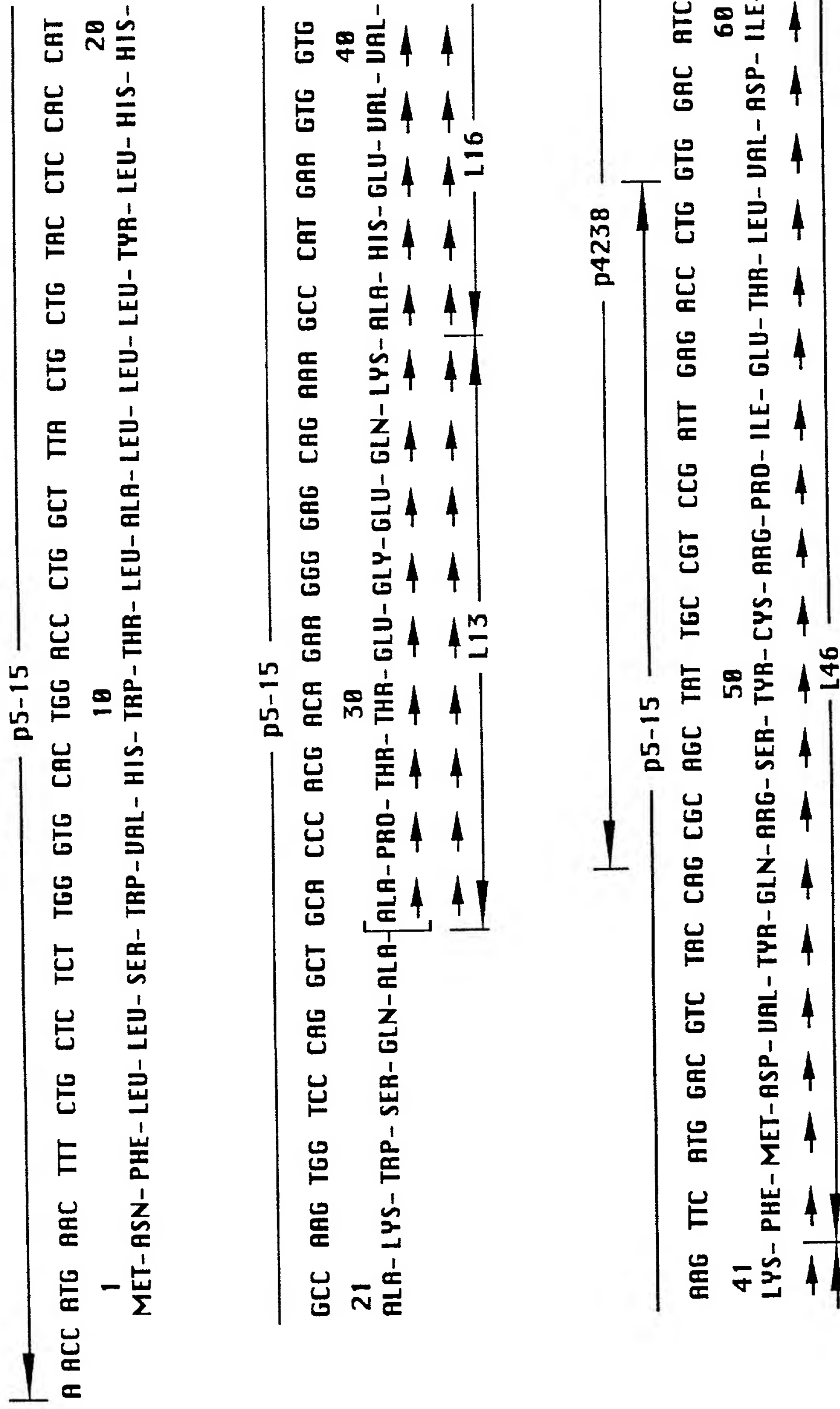


FIG. 4E

p4238  
TTC CAG GAG TAC CCC GAT GAG ATA GAG TAT ATC TTC AAG CCG TCC TGT GTG CCC CTA ATG  
61 70 80  
PHE-GLN-GLU-TYR-PRO-ASP-GLU-ILE-GLU-TYR-ILE-PHE-LYS-PRO-SER-CYS-VAL-PRO-LEU-MET-  
- - - - -

p4238  
CGG TGT GCG GGC TGC TGC AAT GAT GAA GCC CTG GAG TGC GTG CCC ACG TCG GAG AGC AAC  
81 90 100  
ARG-CYS-ALA-GLY-CYS-CYS-ASN-ASP-GLU-GLU-ALA-LEU-GLU-CYS-VAL-PRO-THR-SER-GLU-SER-ASN-  
- - - - -

p4238  
GTC ACT ATG CAG ATC ATG CCG ATC AAA CCT CAC CAA AGC CAG CAC ATA GGA GAG ATG AGC  
101 110 120  
VAL-THR-MET-GLN-ILE-MET-ARG-ILE-LYS-PRO-HIS-GLN-SER-GLN-HIS-ILE-GLY-GLU-MET-SER-  
- - - - -

FIG. 4F

p4238  
TTC CTG CAG CAT AGC AGA TGT GAA TGC AGA CCA ARG AAA GAT AGA ACA AAG CCA GAA AAT 140  
121  
PHE-LEU-GLN-HIS-SER-ARG-CYS-GLU-CYS-ARG-PRO-LYS-LYS-ASP-ARG-THR-LYS-PRO-GLU-ASN-  
L20

pW-3  
p4238  
CAC TGT GAG CCT TGT TCA GAG CCG AGA ARG CAT TTG TTT GTC CAA GAT CCG CAG ACG TGT 160  
141  
HIS-CYS-GLU-PRO-CYS-SER-GLU-ARG-ARG-LYS-HIS-LEU-PHE-VAL-GLN-ASP-PRO-GLN-THR-CYS-  
L30

pW-3  
AAA TGT TCC TGC AAA AAC ACA GAC TCG CGT TGC AAG GCG AGG CAG CTT GAG TTA AAC GAA 180  
161  
LYS-CYS-SER-CYS-LYS-ASN-THR-ASP-SER-ARG-CYS-LYS-ALA-ARG-GLN-LEU-GLU-LEU-ASN-GLU-  
L30 L26

FIG. 4G

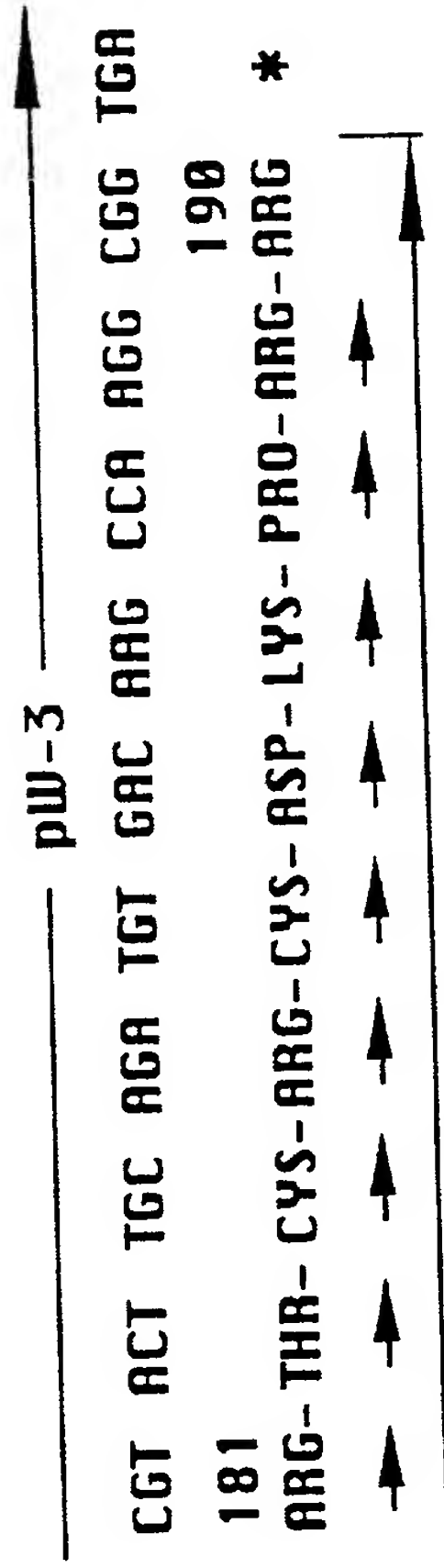


FIG. 4H

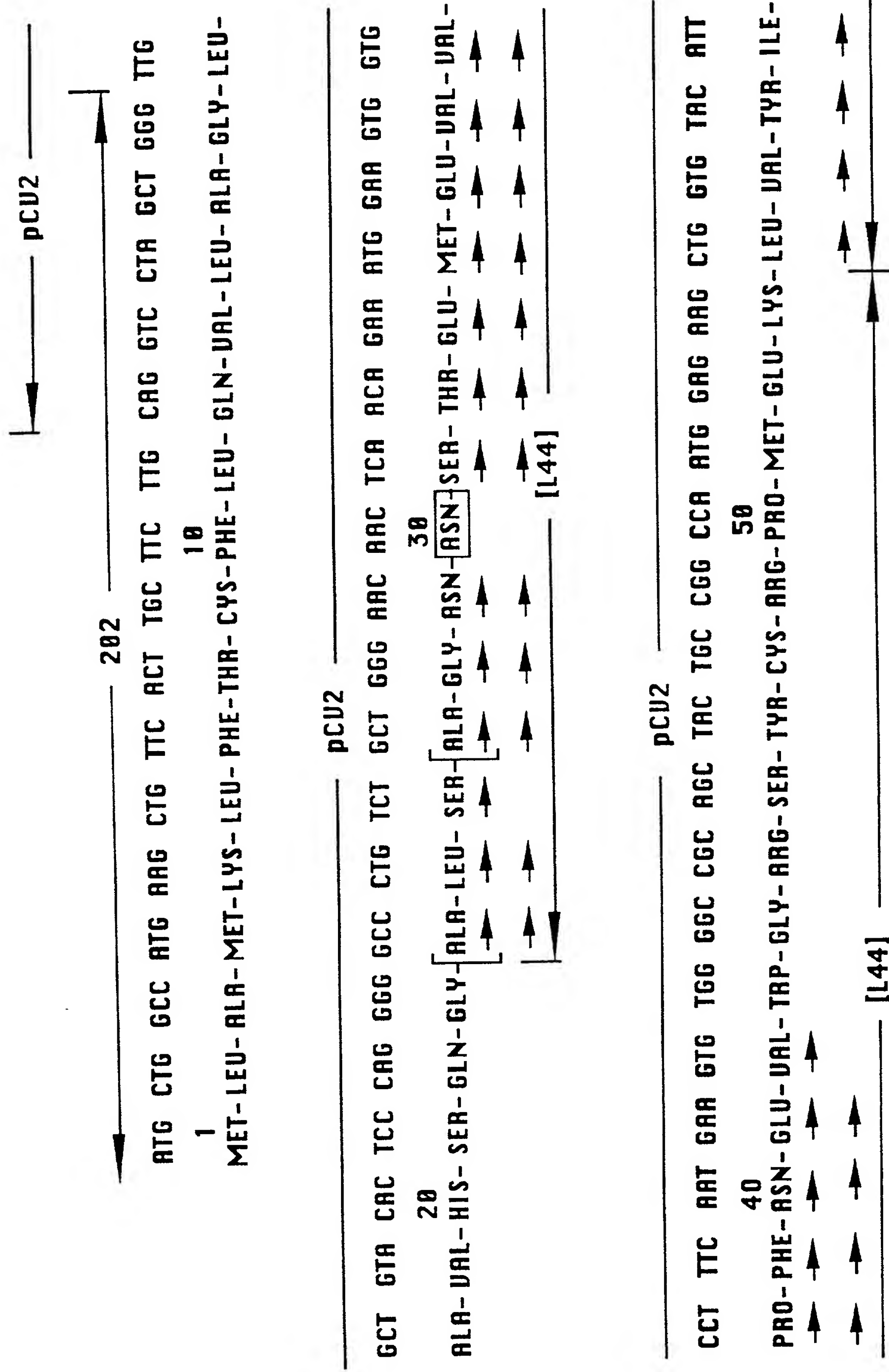


FIG. 4I

89

82

857

88

89

857

**Abstract**

1

198

11

135

L44I

117



ACA TTC TCT CAG GAT GTA CTC TGC GAA TGC AGG CCT ATT CTG GAG ACG ACA ARG GCA GAA  
 120  
 THR-PHE-SER-GLN-ASP-VAL-LEU-CYS-GLU-CYS-ARG-PRO-ILE-LEU-GLU-THR-THR-LYS-ALA-GLU-  
 [L44]

AGG AGG AAA ACC AAG GGG ARG AGG ARG CAA AGC AAA ACC CCA CAG ACT GAG GAA CCC CAC  
 140  
 ARG-ARG-LYS-THR-LYS-GLY-LYS-ARG-LYS-GLN-SER-LYS-THR-PRO-GLN-THR-GLU-GLU-PRO-HIS-  
 150  
 126

CTG TGA  
 158  
 LEU \*

FIG. 4K

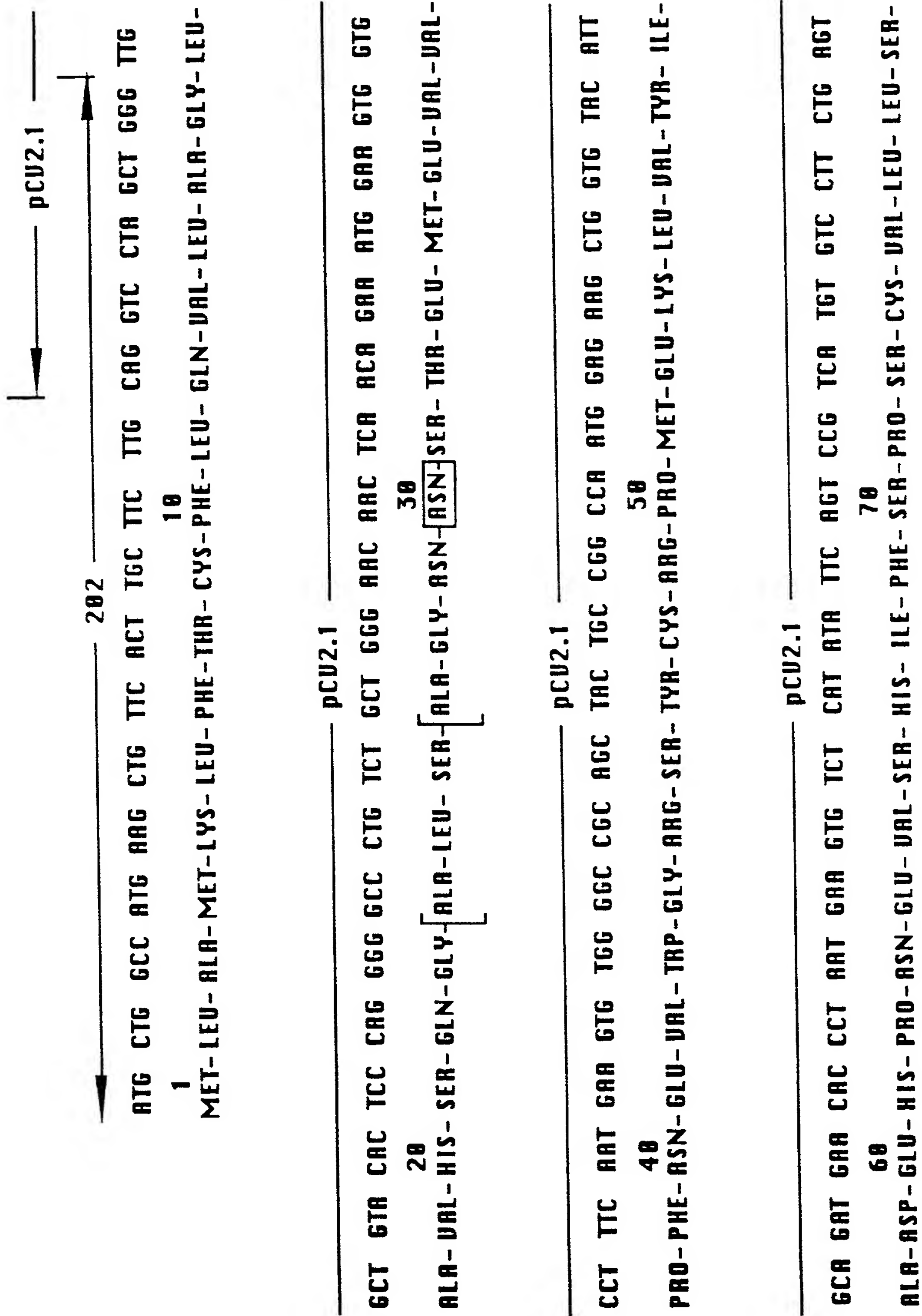


FIG. 4L

PCV2.1  
CGC TGT AGT GGC TGC TGT GGT GAC GAG GGT CTG CAC TGT GTG GCG CTA AAG ACA GCC AAC  
80  
ARG-CYS-SER-GLY-CYS-CYS-GLY-ASP-GLU-GLY-LEU-HIS-CYS-VAL-ALA-LEU-LYS-THR-ALA-ASN

PCV2.1  
ATC ACT ATG CAG ATC TTA AAG ATT CCC CCC AAT CGG GAT CCA CAT TCC TAC GTG GAG ATG  
100  
ILE-THR-MET-GLN-ILE-LEU-LYS-ILE-PRO-PRO-ASN-ARG-ASP-PRO-HIS-SER-TYR-VAL-GLU-MET

PCV2.1  
ACA TTC TCT CAG GAT GTA CTC TGC GAA TGC AGG CCT ATT CTG GAG ACG ACA AAG GCA GAR  
120  
THR-PHE-SER-GLN-ASP-VAL-LEU-CYS-GLU-CYS-ARG-PRO-ILE-LEU-GLU-THR-THR-LYS-ALA-GLU



AGG TAA

138

ARG \*

FIG. 4M

A ACC ATG AAC TTT CTG CTC TCT TGG GTG CAC TGG ACC CTG GCT TTA CTG CTG TAC CTC CAC CAT  
 10  
 MET-ASN-PHE-LEU-LEU-SER-TRP-DAL-HIS-TRP-LEU-ALA-LEU-LEU-LEU-TYR-LEU-HIS-HIS-

GCC AAG TGG TCC CAG GCT GCA CCC ACG ACA GAA GGG GAG CAG AAA GCC CAT GAA GTG GTG  
 30  
 ALA-LYS-TRP-SER-GLN-ALA-ALA-PRO-THR-THR-GLU-GLY-GLU-GLN-LYS-ALA-HIS-GLU-DAL-DAL-  
 40  
 L13 L16

AAG TTC ATG GAC GTC TAC CAG CGC AGC TAT TGC CGT CCG ATT GAG ACC CTG GTG GAC ATC  
 50  
 LYS-PHE-MET-ASP-DAL-TYR-GLN-ARG-SER-TYR-CYS-ARG-PRO-ILE-GLU-THR-LEU-DAL-ASP-ILE-  
 60  
 L46

FIG. 5

p4238

CGG TGT GCG GGC TGC TGC AAT GAT GAA GCC CTG GAG TGC GTG CCC ACG TCG GAG AGC AAC  
81  
ARG-CYS-ALA-GLY-CYS-CYS-ASN-ASP-GLU-ALA-LEU-GLU-CYS-VAL-PRO-THR-SER-GLU-SER-ASN-100

146

p4238

GTC ACT ATG CAG ATC ATG CCG ATC AAA CCT CAC CAA AGC CAG CAC ATA GGA GAG ATG AGC  
101 110 120  
VAL-THR-MET-GLN-ILE-MET-ARG-ILE-LYS-PRO-HIS-GLN-SER-GLN-HIS-ILE-GLY-GLU-MET-SER-

L46

**FIG. 5A**

pW-3  
 p4238  
 CAC TGT GAG CCT TGT TCA GAG CCG AGA ARG CAT TTG TTT GTC CAA GAT CCG CAG ACG TGT  
 141  
 HIS-CYS-GLU-PRO-CYS-SER-GLU-ARG-ARG-LYS-HIS-LEU-PHE-VAL-GLN-ASP-PRO-GLN-THR-CYS-  
 150  
 160  
 L30

AAA TGT TCC TGC AAA AAC ACA GAC TCG CGT TGC AAG GCG AGG CAG CTT GAG TTA AAC GAA  
 161 170 180  
 LYS-CYS-SER-CYS-LYS-ASN-THR-ASP-SER-ARG-CYS-LYS-ALA-ARG-GLN-LEU-GLU-LEU-ASN-GLU-  
 L26 L30

**FIG. 5B**

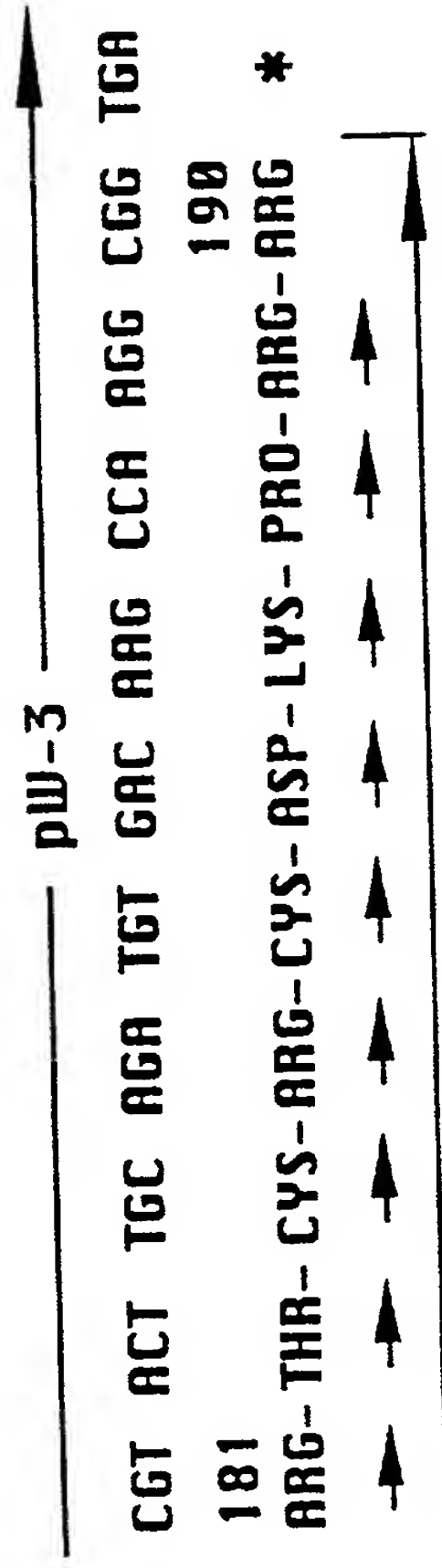
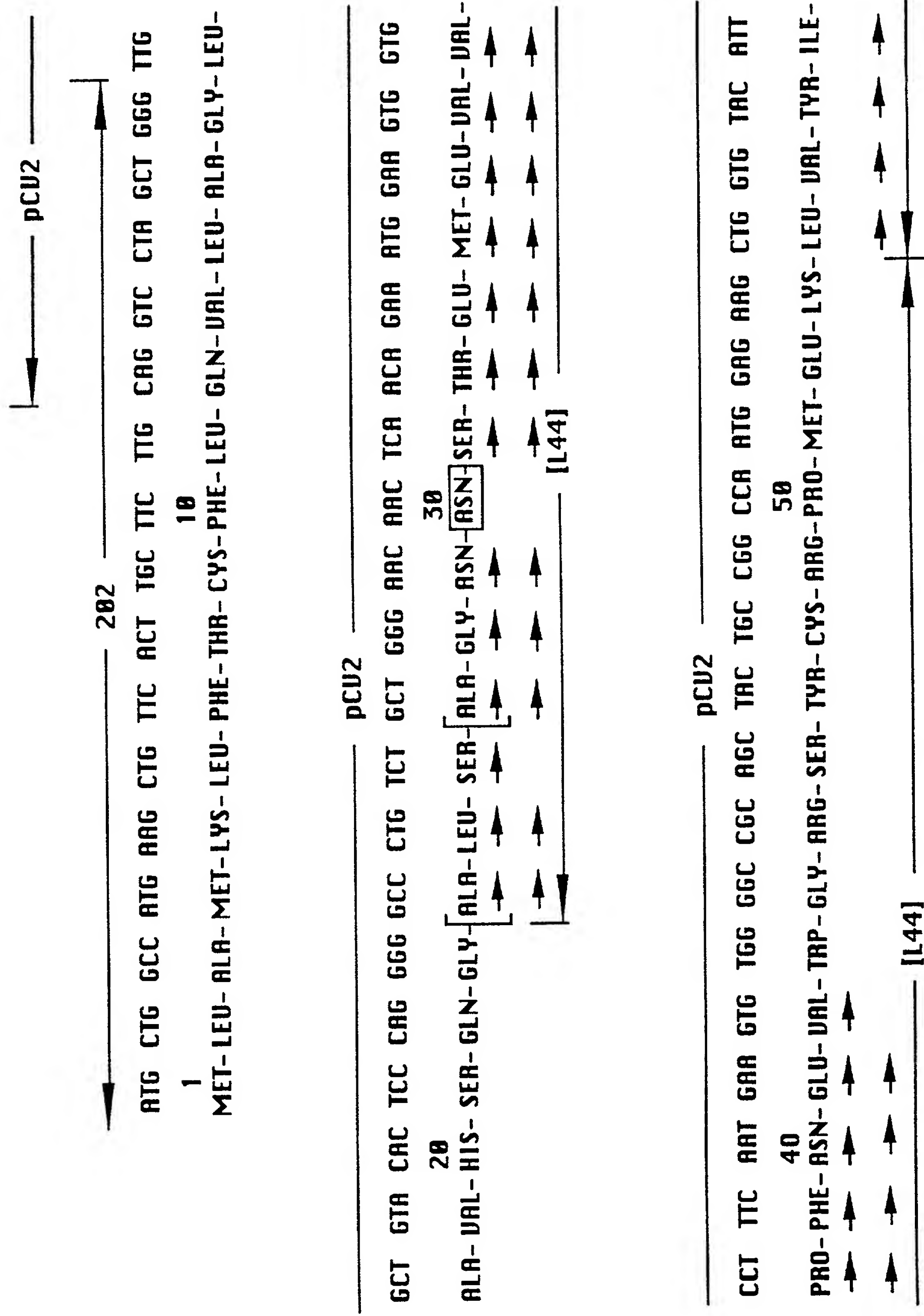


FIG. 5C



**FIG. 6**



PCU2  
 GCA GAT GAA CAC CCT AAT GAA GTG TCT CAT ATA TTC AGT CCG TCA TGT GTC CTT CTG AGT  
 60  
 ALA-ASP-GLU-HIS-PRO-ASN-GLU-VAL-SER-HIS-ILE-PHE-SER-PRO-SER-CYS-VAL-LEU-LEU-SER-  
 70  
 150

PCU2  
 CGC TGT AGT GGC TGC TGT GGT GAC GAG GGT CTG CAC TGT GTG GCG CTA AAG ACA GCC AAC  
 80  
 ARG-CYS-SER-GLY-CYS-CYS-GLY-ASP-GLU-GLY-LEU-HIS-CYS-VAL-ALA-LEU-LYS-THR-ALA-ASN-  
 90  
 150

PCU2  
 ATC ACT ATG CAG ATC TTA AAG ATT CCC AAT CGG GAT CCA CAT TCC TAC GTG GAG ATG  
 100  
 ILE-THR-MET-GLN-ILE-LEU-LYS-ILE-PRO-PRO-ASN-ARG-ASP-PRO-HIS-SER-TYR-VAL-GLU-MET-  
 110  
 135 [144]

FIG. 6A

CTG TGA  
158  
LEU \*

PCU2

AGG AGG AAA ACC AAG GGG AAG AGG CAA AGC AAA ACC CCA CAG ACT GAG GAA CCC CAC

140

ARG-ARG-LYS-THR-LYS-GLY-LYS-ARG-LYS-GLN-SER-LYS-THR-PRO-GLN-THR-GLU-GLU-PRO-HIS-

150

126

**FIG. 6B**

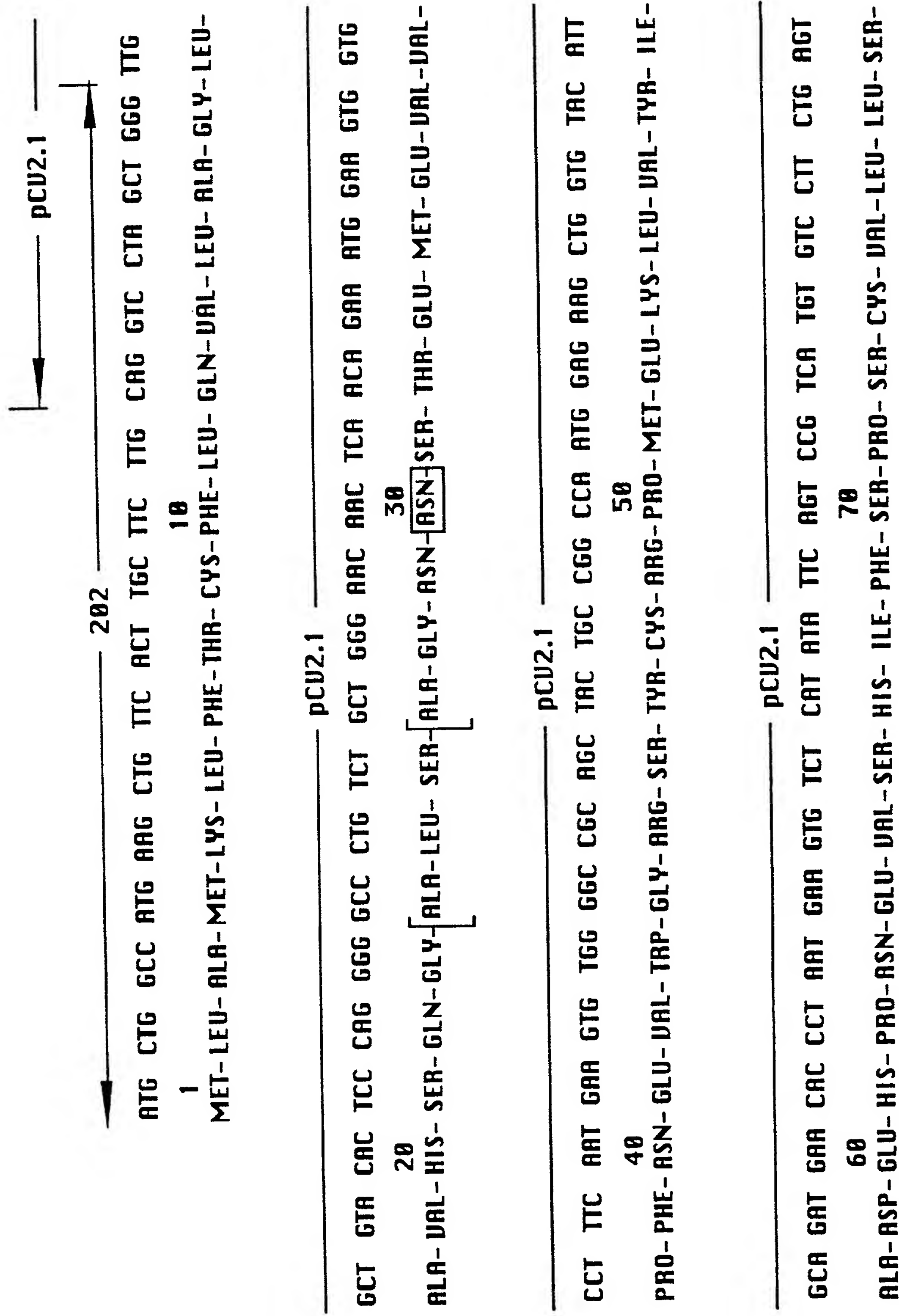


FIG. 7

PCV2.1  
 CGC TGT AGT GGC TGC TGT GGT GAC GAG GGT CTG CAC TGT GTG GCG CTA AAG ACA GCC AAC  
 80  
 ARG-CYS-SER-GLY-CYS-CYS-GLY-ASP-GLU-GLY-LEU-HIS-CYS-DAL-ALA-LEU-LYS-THR-ALA-ASN

PCV2.1  
 ATC ACT ATG CAG ATC TTA AAG ATT CCC CCC AAT CGG GAT CCA CAT TCC TAC GTG GAG ATG  
 100  
 ILE-THR-MET-GLN-ILE-LEU-LYS-ILE-PRO-PRO-ASN-ARG-ASP-PRO-HIS-SER-TYR-DAL-GLU-MET-

PCV2.1  
 ACA TTC TCT CAG GAT GTA CTC TGC GAA TGC AGG CCT ATT CTG GAG ACG ACA AAG GCA GAA  
 120  
 THR-PHE-SER-GLN-ASP-DAL-LEU-CYS-GLU-CYS-ARG-PRO-ILE-LEU-GLU-THR-THR-LYS-ALA-GLU-



AGG TAA

138

ARG \*

FIG. 7A

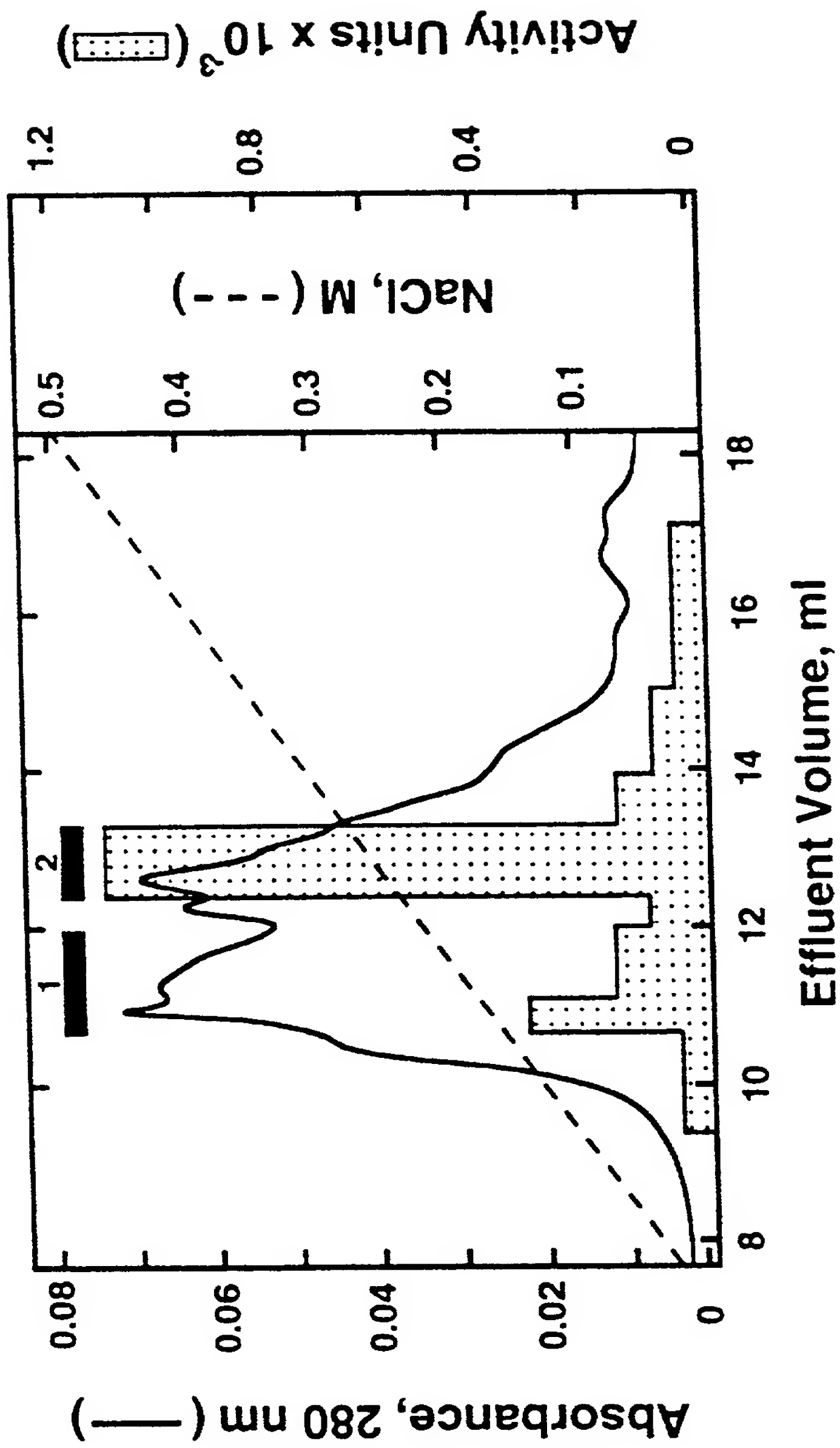


FIG. 8A

208020" 04ET200T

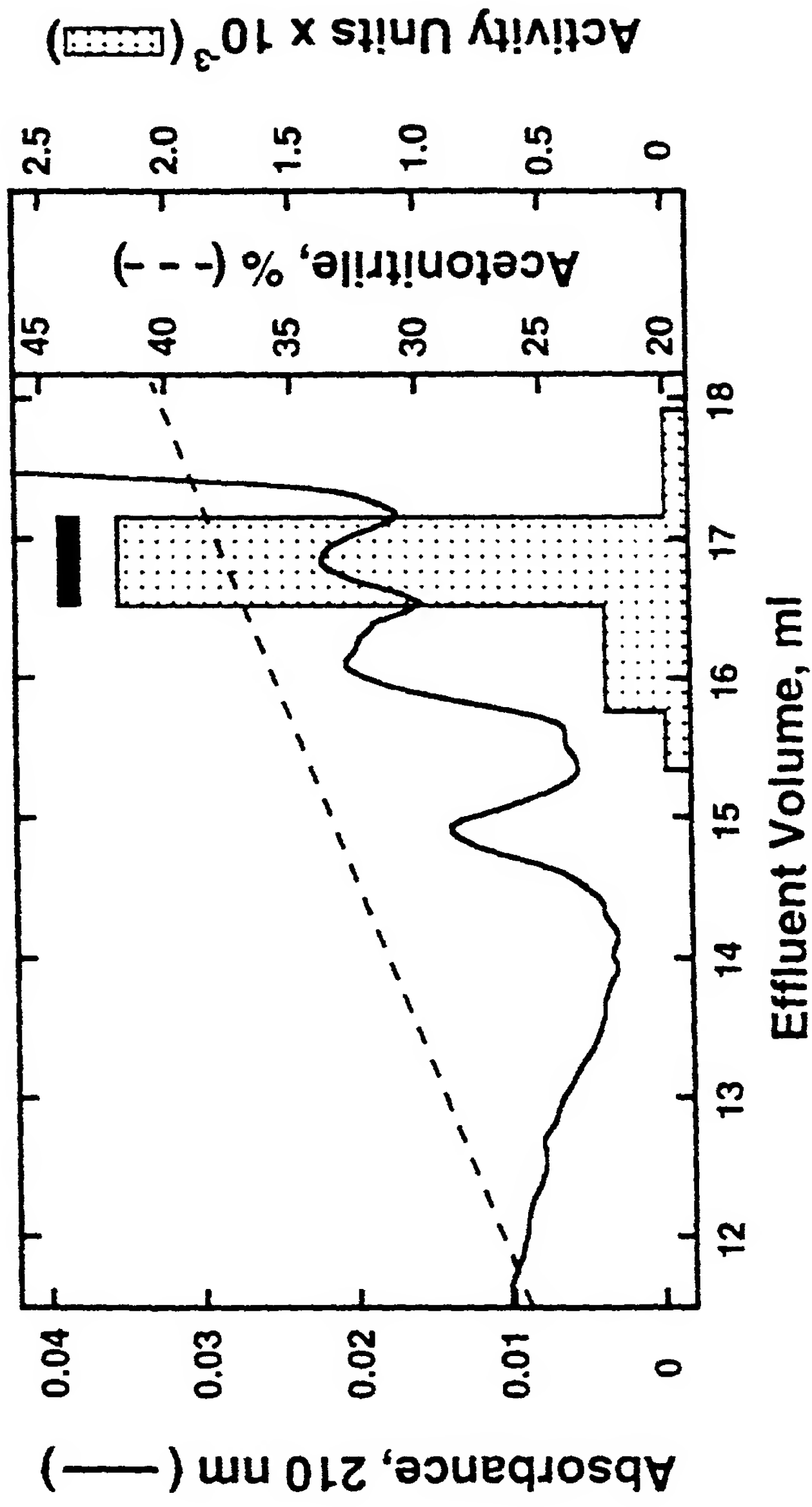


FIG. 8B

208020" 0/ET<00F

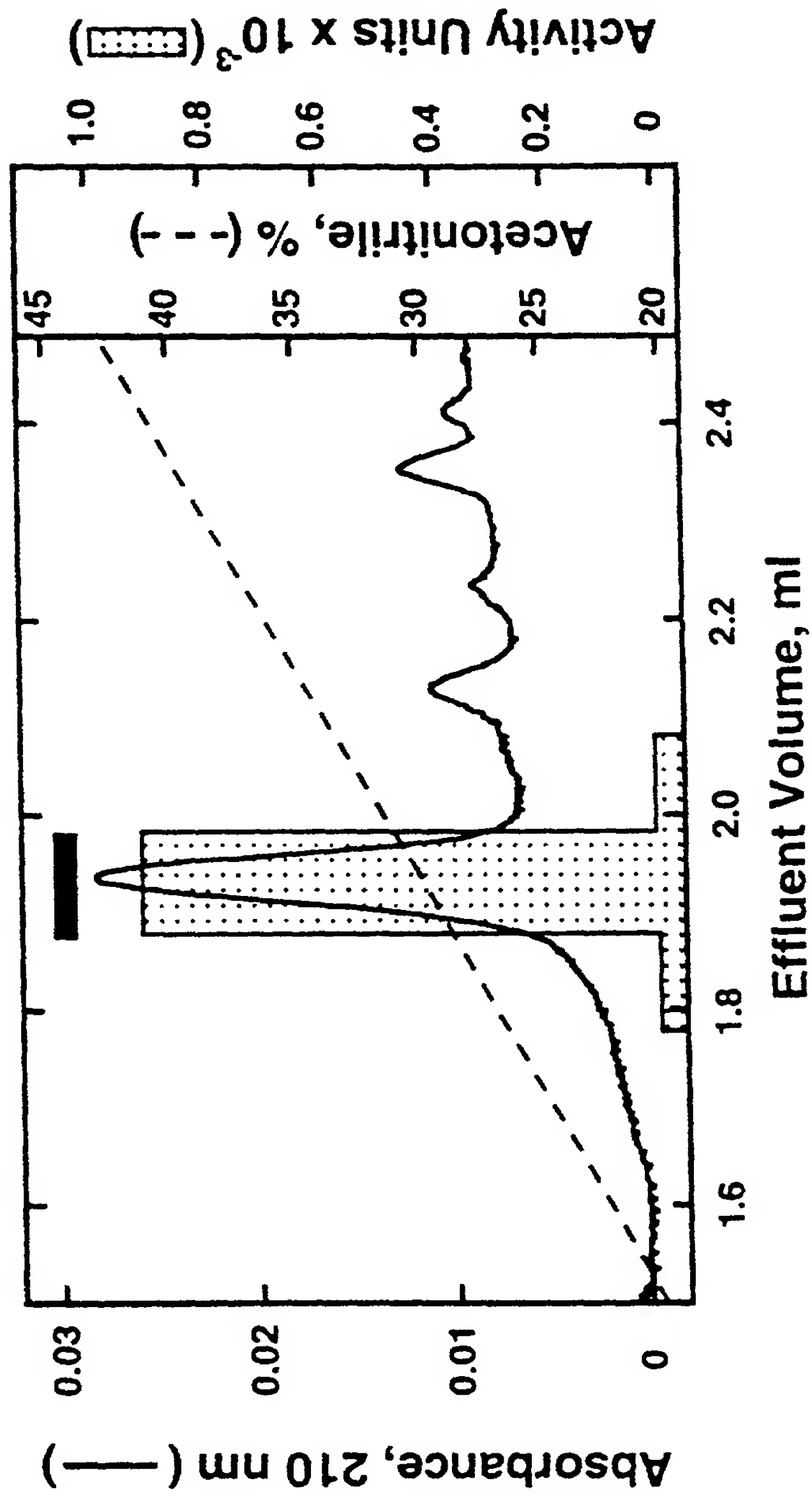


FIG. 8C

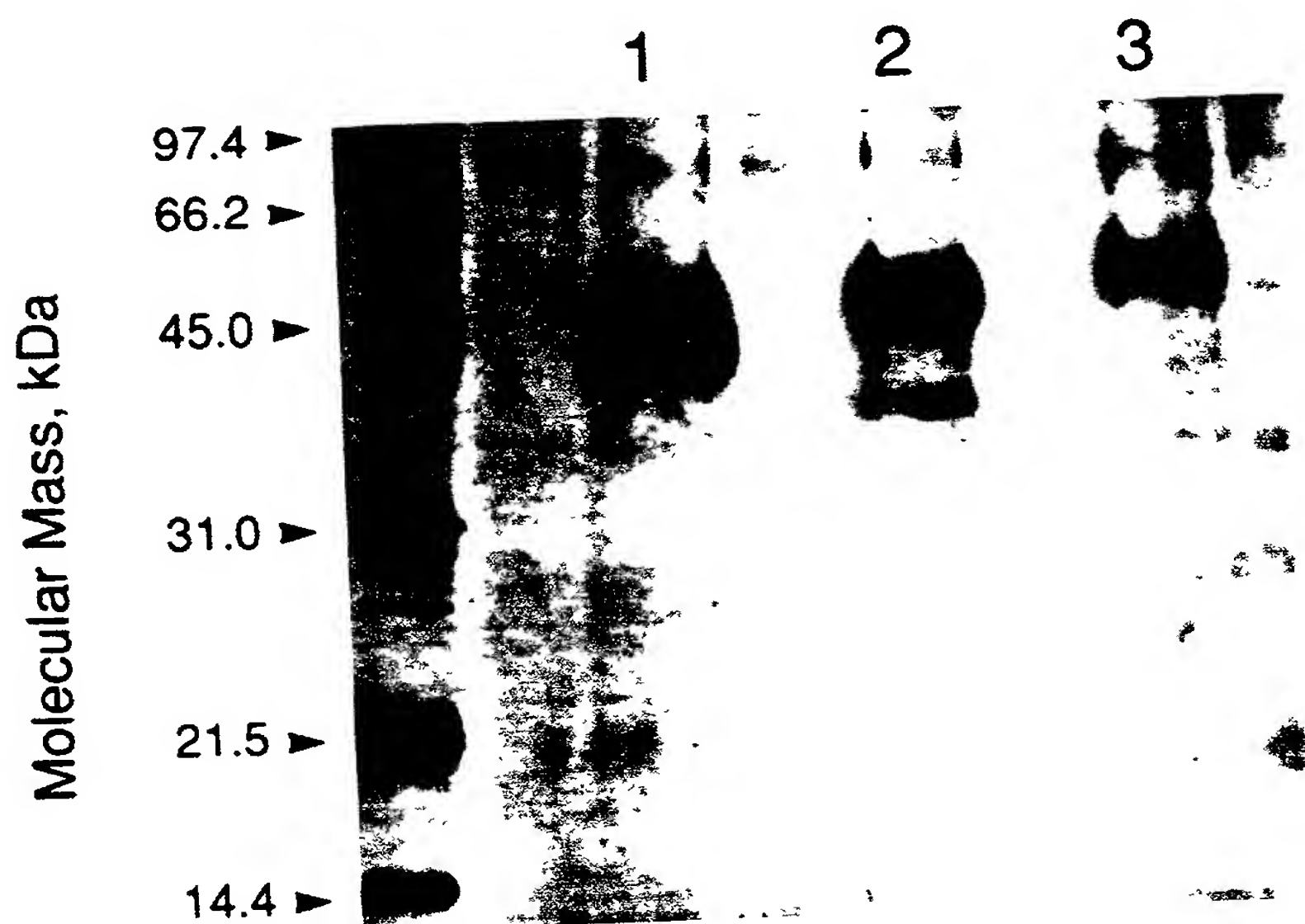


FIG.9A

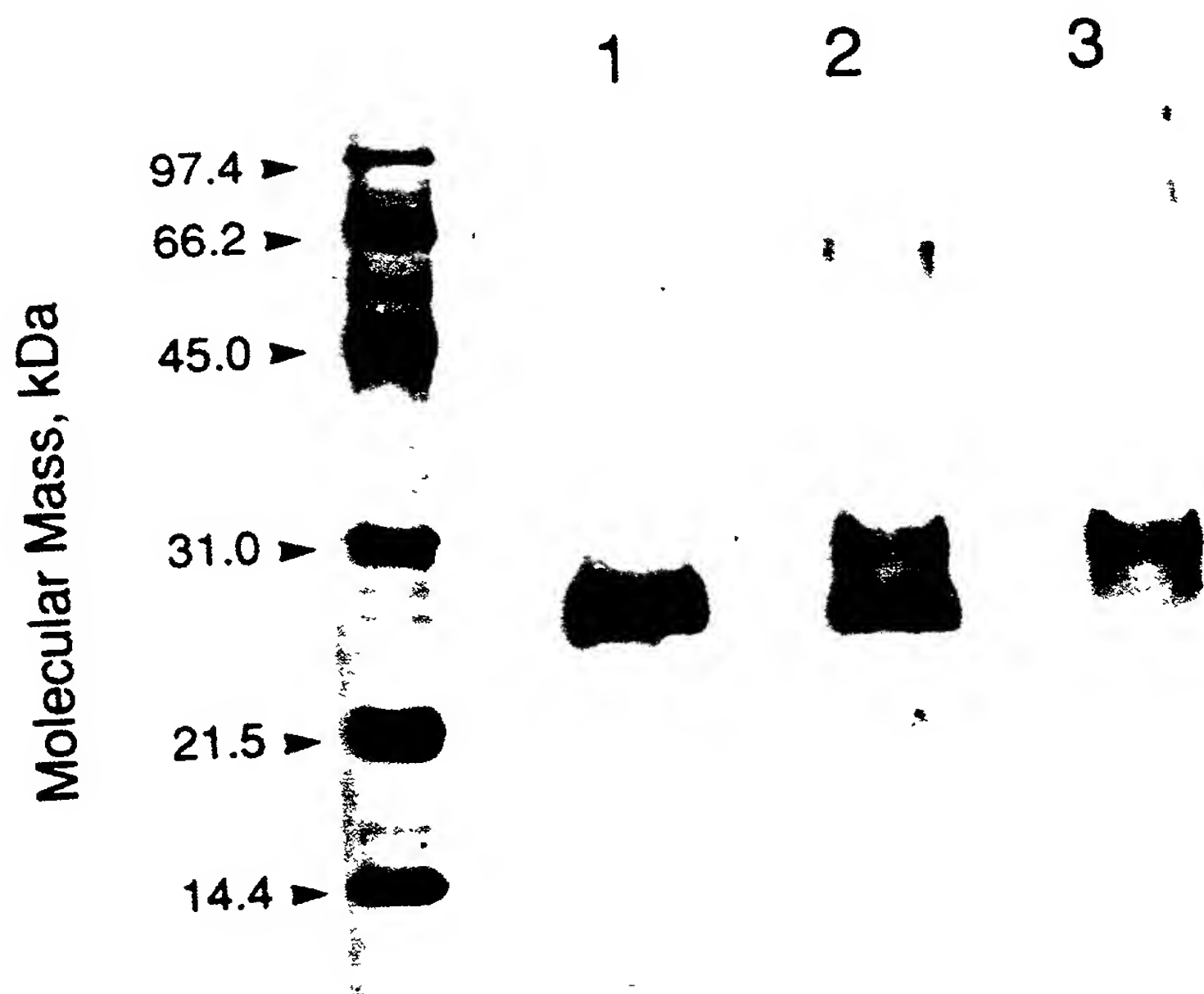


FIG.9B



208020-0/ET/001

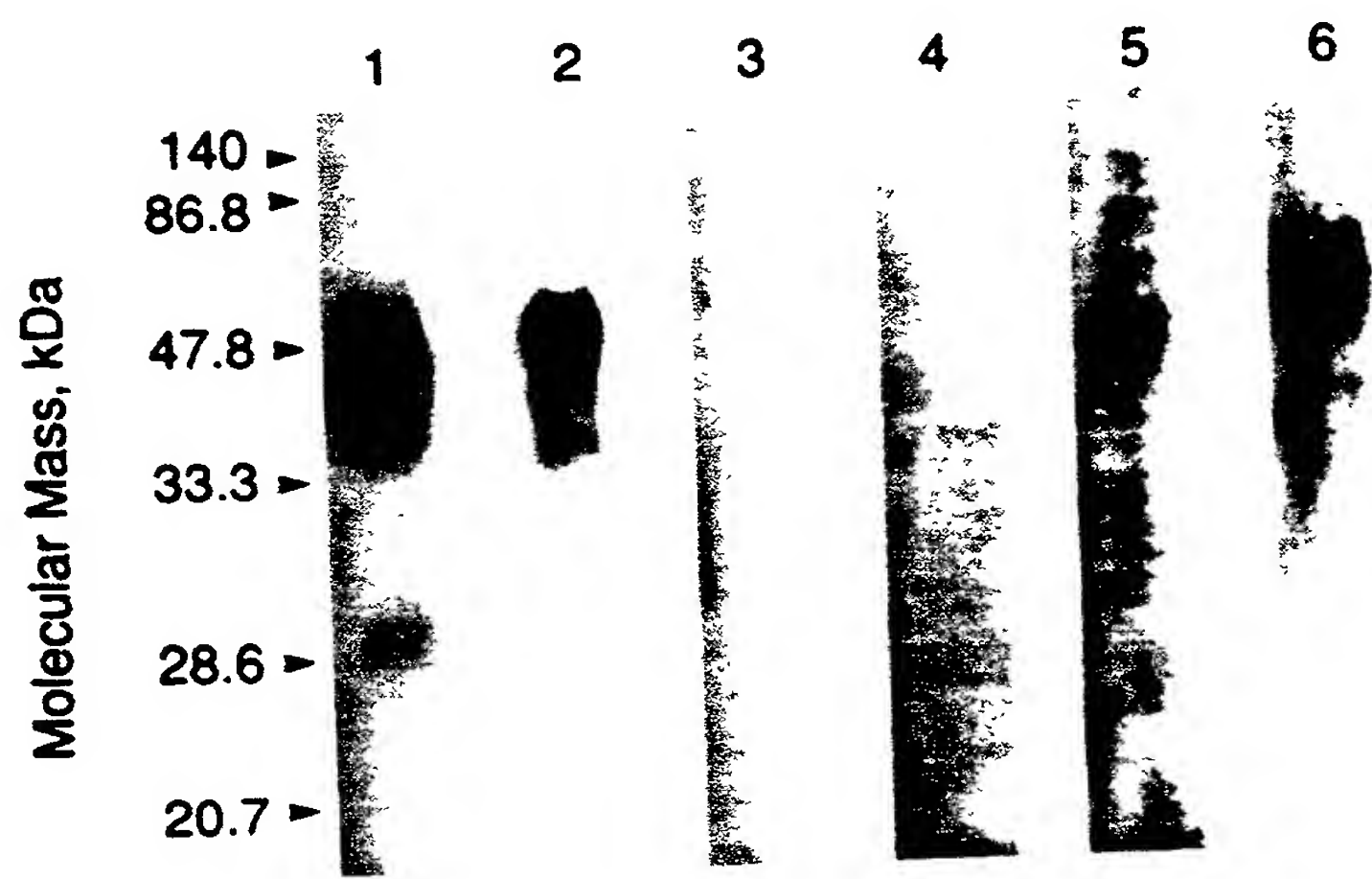


FIG. 10A

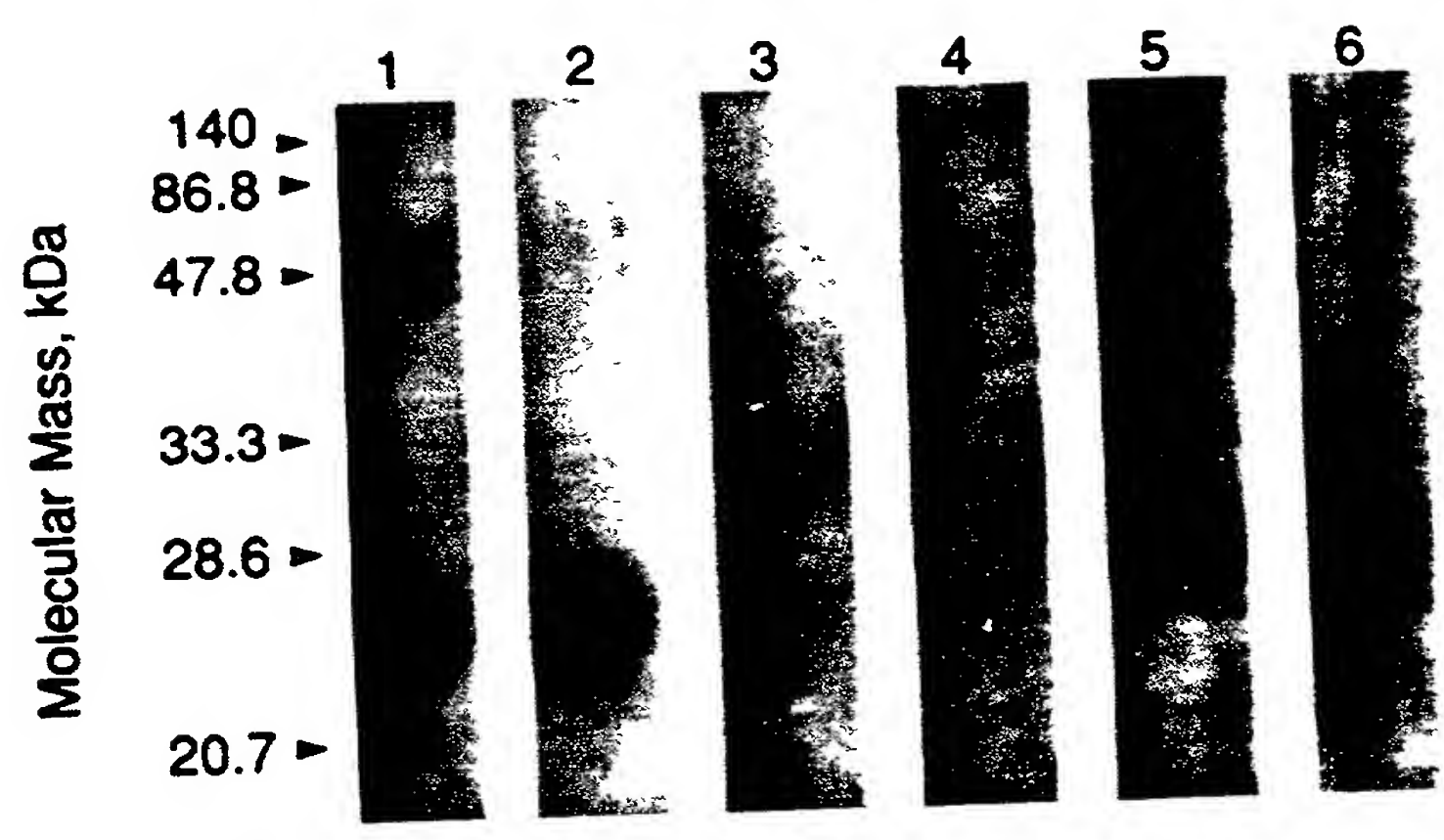
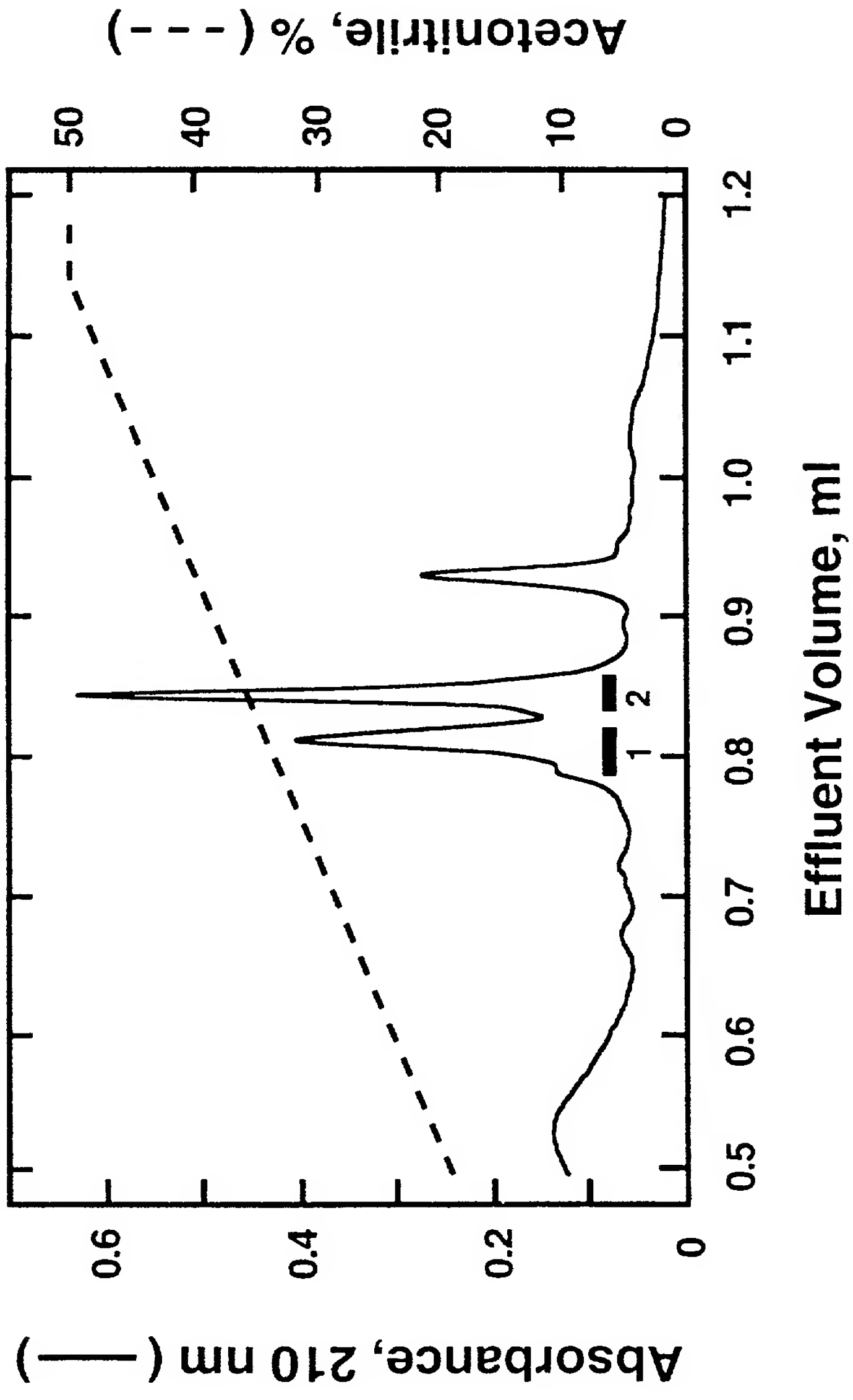


FIG. 10B

[illegible]

**FIG. 11**